PUBLICATIONS - continued

Mary Stearns Parshley

32.	Parshley, M. S.	Enzymatic destruction of growth inhibitors. Excerpta Med., 19, Sec.I, XXXV, Oct. 1965.
33.	Parshley, M. S., Blackwood, C. E., and Mandl, I.	Specific tumor inhibitors from normal tissue. Proc. Am. Assn. Cancer Res., 6:50, 1965.
34.	Parshley, M. S., and Mandl, I.	Inhibition of malignant cells in vitro by a component of normal adult connective tissue. Nature, 208:800, Nov. 1965.
35.	Parshley, M. S., Mandl, I., and Manahan, J.	Separation and in vitro study of tumor cell inhibitors. Proc. Tissue Culture Assn., San Francisco, June, 1966. In Vitro, 2:124, 1966.
36.	Levi, M., Mandl, I., Parshley, M. S., and Swartz, D. P.	Antibody to papillary cystadenocarcinoma of the ovary. Proc. Pan American Cancer Cytology Congress, May 1967, New York City.
37.	Levi, M., Parshley, M., and Mandl, I.	Antigenicity of ovarian carcinoma cells grown in tissue culture. Proc. Tissue Culture Assn., June 1967, Philadelphia.
38.	Martorelli, Braz, Jr., Parshley, M. S., and Moore, J. G.	Effect of chemotherapeutic agents on a line of human breast carcinoma cells in tissue culture. Proc. Tissue Culture Assn., May 1967, Philadelphia.

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Other Sources of Financial Support

List financial support for research from all sources, including own institution, for this and/or related research projects.

	Title of Project	Source	Amount	Duration
Current	Study of Naturally Occurring Growth Inhibitors	National Cancer Institute	$ 28,736	to 12/31/67
	Growth Inhibition of Malignant Cells in vitro and in vivo	Damon Runyan Memorial Fund	20,900	to 2/29/68
Pending	Effect of Vinca alkaloids on Human Neoplastic Cells in tissue culture	Leukemia Society, Inc. Scholarship	75,000	Jan. 1, 1968 to Dec. 31, '72
	Biology and Chemistry of Cultured Ovarian Cancer Cells	National Cancer Institute	50,445	Jan. 1, 1968 to Dec. 31, 1970

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PUBLICATIONS - MARY STEARNS PARSHLEY

1. Stearns, Mary L. — Growth and differentiation of connective tissue as observed microscopically in the living rabbit. Am. J. Med. Sci. 198:144-145, 1939. Proc. Phys. Soc., Phila., 14:20-21, 1938-1939.

2. Stearns, Mary L. — Growth and differentiation of connective tissue as observed microscopically in the living rabbit. Anat. Rec. 73:3, 1939 Suppl. 2, p.49 (abstract).

3. Stearns, Mary L. — Studies on the development of connective tissue in transparent chambers in the rabbit's ear. I. Am. J. Anat. 66: 133-176, 1940.

4. Stearns, Mary L. — Studies on the development of connective tissue in transparent chambers in the rabbit's ear. II. Am. J. Anat. 67: 55-97, 1940.

5. Parshley, M.S., and Simms, H.S. — Conditions favoring the growth of adult skin epithelium in vitro. Anat. Rec. 94:3:486, 1946 (abstract).

6. Simms, H. S., and Parshley, M. S. — Studies on the fat depositing mechanism. Proc. Am. Soc. Study Arteriosclerosis. Am. Heart J. 35:860-861, 1947.

7. Simms, H. S., Parshley, M. S., and Pitt, R. B. — Fat deposition in vitro caused by lipfanogens and opposed by antilipfanogen. J. Geront. 2:3:205-216, 1947.

8. Simms, H. S., Parshley, M. S., Pitt, R. B., and Fulton, J. B. — Further studies on the fat depositing mechanism in vitro. Am. Heart J. 36: 469, 1948 (abstract).

9. Fulton, J. B., Parshley, M. S., Simms, H. S. — Growth of blood vessels from adult tissue in vitro. Anat. Rec. 103-453, 1949 (abstract).

10. Parshley, M. S., and Simms, H. S. — Cultivation of adult skin epithelial cells, chicken, and human, in vitro. Am. J. Anat. 86:163-190, 1950.

11. Parshley, M. S., and Deterling, R. A., Jr., and Coleman, C. C., Jr. — Cultivation in vitro of fresh and frozen segments of the abdominal aorta of the dog. Anat. Rec. 106:64, 1950, (abstract).

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Source: https://www.industrydocuments.ucsf.edu/docs/yxwm0000

6. cont. Pertinent Literature References

1. Crocker, T. T., Nielson, B. I., and Laznitski, I. Carcinogenic hydrocarbons. Arch. of Environ. Health, 10:2:240, 1965.

2. ----------, and Nielson, B. I. Effects of carcinogenic and non-carcinogenic hydrocarbons on respiratory epithelium in orhan culture. Tissue Culture Assn. Proc., Miami, June, 1965, p. 56.

3. Dawson, F. W. Effects of nicotine and influenza on human ciliary activity in vitro. Fed. Am. Soc. Exp. Biol. and Med. Proc., 24: part I, #260, 1965.

4. Kensler, C. J. The pharmacology of tobacco smoke effects of chronic exposure. in "Tobacco and Health", ed. by G. James and T. Rosenthal, Chap. 1, Charles Thomas, Springfield, Ill. 1962, p. 5.

5. Laznitski, I. Effect of 3,4-Benzpyrene on human foetal lung grown in vitro. Brit. J. Cancer, 10:510, 1956.

6. ---------- Observations on the effects of condensates from cigarette smoke on human foetal lung in vitro. Brit. J. Cancer, 12:547, 1958.

7. Leuchtenberger, C., and Leuchtenberger, R. A correlated histological, cytological, and cytochemical study of the major bronchi from mice exposed to cigarette smoke. in "Tobacco and Health", ed. by G. James and T. Rosenthal, Chap. 8, Charles Thomas, Springfield, Ill. 1962, p. 81.

8. Lindsey, A. J. Some observations upon the chemistry of tobacco smoke. in "Tobacco and Health", ed. by G. James and T. Rosenthal, Chap. 2, Charles Thomas, Springfield, Ill., 1962, p. 21.

9. Nielson, B. I., and Crocker, T. T. Epithelial and mesenchymal interactions in hamster respiratory mucosa exposed to polycyclic hydrocarbons in organ culture. Tissue Culture Assn. Proc., Philadelphia, June, 1967, p. 15.

10. Pace, D. M., and Elliott, A. Studies on the effect of acetaldehyde on tissue cells cultivated in vitro. Cancer Res., 20:868, 1960.

11. ----------, Thompson, J. R., Aftonomos, B., and Holck, G. O. Effects of NO_2 and salts of NO_2 on established cell lines. Canad. J. Biochem. and Phys., 39:1247, 1961.

12. ----------, Aftonomos, B., Elliott, A., and Sommer, S. Observations on some effects of the sodium salts of certain monocarboxylic acids on established cell lines. Canad. J. Biochem., 45:81, 1967.

13. Rounds, D. E., and Bils, R. F. Effects of air pollution on cells in culture. Arch. Environ. Health, 10:251, 1965.

14. Stevens, K. M. Lung cancer, an evolutionary approach. Austral. J. Exp. Biol. and Med. Sci., 43:421, 1965.

15. Wynder, E. L., Hoffmann, D., and Auerbach, O. The role of particulate and volatile components in tobacco carcinogenesis. Am. Assn. Cancer Res., 6:69, 1965.

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6. cont.
may be caused by an interference on the part of some of these volatile constituents of tobacco and polluted air with the oxygen supply to these cells necessary for aerobic respiration. This anoxia could result in a mutation toward anaerobic glycolysis as a source of energy characteristic of bronchogenic carcinoma (14).

The technique of tissue culture makes possible the direct observation of human tissues under high magnifications. The biological effect of whole tobacco smoke as well as some of its volatile constituents on these cells can be studied microscopically, and the metabolic byproducts of the cells under different conditions can be analyzed. Cell lines provide a source of uniform test material. In addition test materials can be added in a concentration not possible in the intact animal and under conditions of prolonged contact permitting the equilibrium of poorly soluble or slowly diffusing substances between the medium and the cells. A number of materials possibly related to a neoplastic activity of either tobacco smoke or polluted air have been studied by this method. Hyperplasia and metaplasia considered preneoplastic in cultures of human foetal lung treated with polycyclic hydrocarbons and tobacco smoke condensate and its fractions was reported by Laznitski (5,6). Crocker and coworkers havecarried on similar studies with rat and hamster trachea in tissue culture (1,2,9). These workers reported a nonspecific effect of these carcinogens, and also that analogs of these hydrocarbons not known to be carcinogenic produced similar abnormalities in cultures of respiratory epithelium. Toxic effects of organic constituents of tobacco smoke and polluted air, acetaldehyde, nitrogen dioxide, and monocarboxylic acids, on lines of human and animal cells in tissue culture were observed by Pace and his coworkers. (10,11,12). Rounds also observed that nitrogen dioxide introduced as sodium nitrite into the medium of cultures of trypsinized and suspended cells from the lungs of mice and rats caused nuclear and cytoplasmic changes which accompanied a reversible inhibition of respiratory activity (13).

See continuation sheet 1b for Pertinent Literature Ref, cited above.

It is proposed to study the effect of some of the gaseous constituents of tobacco smoke and polluted air on established lines of normal and malignant human respiratory epithelium from the pharynx, larynx, and lung and to compare their characteristics as evidenced in tissue culture under these experimental conditions. Effect on rate of proliferation, cell movement and contact relationship, nuclear and cytoplasmic structure and chromosome content will be correlated with differences in metabolic activity and related to neoplastic capability. A clear understanding of the morphological and metabolic differences between normal and malignant human respiratory epithelium should contribute to an understanding of the neoplastic process itself..

7.,cont.
of these conditions in tissue cultures of these cells by a manipulation of the gaseous atmosphere of the culture should demonstrate this. Similar experimentation with the gaseous phase over respiratory cancer cells in tissue culture might lead to changes in the morphologic and metabolic characteristics of these altered cells which could give a clue to the causes of carcinogenesis. These studies have a direct bearing on neoplastic development and the biological and biochemical mechanisms responsible.

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13. Budget: (1st year)

A. Salaries (Personnel by names)	% time	Amount
Professional		
Technical		
Research Assistant	100	R
Diener	50	
Fringe Benefits (10)		
	Sub-Total	R
B. Consumable Supplies (list by categories)		
Special glassware and equipment for tissue culture		$ 1,000
Media, chemicals, and stains		1,000
	Sub-Total	$ 2,000
C. Other Expenses (itemize)		
Travel to scientific meetings		$ 500
	Sub-Total	$ 500
D. Permanent Equipment (itemize)		
Zeiss Photomicroscope		$ 5,820
Mark Scholander Respirometer		975
E. Overhead (15% of A+B+C)		$ 1,744.50
	Total	$20,169.50

Estimated Future Requirements:

	Salaries	Consumable Suppl.	Other Expenses	Permanent Equip.	Overhead	Total
Year 2	R	$ 2,000	$ 500		$ 1,835	$14,070
Year 3		$ 2,000	$ 500		$ 1,910	$14,640

It is understood that the applicant and institutional officers in applying for a grant have read and found acceptable the Council's "Statement of Policy Containing Conditions and Terms Under Which Project Grants Are Made."

Signature Mary L. Parshley
Director of Project
Telephone

Signature [illegible]
Business Officer of the Institution
VICE-PRESIDENT IN CHARGE OF MEDICAL AFFAIRS
Telephone

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8. Details of Experimental Design and Procedures: (Attach Separate Pages)

It is planned to maintain the following lines of normal and malignant human respiratory epithelium as monolayers of cells on glass in milk dilution bottles in mixtures of serum (human placental, horse, and calf) in synthetic media, Parker's Medium 199 or Eagle's minimal essential medium (MEM) under an atmosphere of 5% CO_2 in air.

a. Line KB, human epidermoid carcinoma of the pharynx
b. Line H.Ep.#2, human epidermoid carcinoma of the larynx, carried in our laboratory.
c. Line L-132, normal human fetal lung epithelium

We also intend to set up other lines of freshly explanted normal and malignant human epithelium from biopsy material which will be obtained through the cooperation of Dr. Sheldon C. Sommers, Professor of Pathology at Delafield Hospital. These lines will be used to compare the effect of the experimental conditions on freshly explanted tissue as opposed to the older lines.

Experiments to determine the effect of tobacco smoke and some of its volatile components will be carried out as follows. At intervals series of tubes with and without coverslips will be seeded with a known number of cells. After the cells have become confluent the medium will be renewed and the cultures will be gassed by means of an apparatus used routinely in our laboratory for adjusting the gaseous phase of the culture with mixtures of O_2, CO_2, N_2, and NO_2 for short periods. In other experi-

(cont. on p. 2a)

9. Physical Facilities Available (Where Other than Administering Organization Indicate Geographical Location)

Large well-equipped tissue culture laboratory with glass enclosed sterile room, incubators, refrigerators, deep-freezes, large and small centrifuges, Mettler microanalytical balances, torsion balances, Leitz Ortholux research microscope with equipment for bright light and phase contrast microscopy, Zeiss inverted research microscope with some light and phase contrast equipment, Leitz binocular microscope with Leitz Micros Time attachment for photography with lightmeter, camera back, and other equipment for microphotography and microscopy, sterilizers, stills, special glassware and equipment for Carrel flask, Maximow slide, Leighton tube, and bottle culture, equipment for histological and histochemical studies.

10. Additional Requirements:

The chemical investigation will be carried out in collaboration with Dr. Ines Mandl who has several rooms in Delafield Hospital equipped for biochemical analysis and separation, including cold room, deep freezes, refrigerators, freezer-dryers, analytical balances, homogenizers, two high speed ultracentrifuges, chromatographic and electrophoretic equipment, Spinco L2 ultracentrifuge with swinging bucket, and Elphor FF electrophorator. Dr. Mandl is Asst. Professor of Biochemistry in Obstetrics & Gynecology.

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11. Biographical sketches of all principal and professional personnel (append)

See attached curriculum vitae.

12. List of publications: (Five most recent as pertinent) (append)

See attached continuation sheet 2b.

Source: https://www.industrydocuments.ucsf.edu/docs/yxwm0000

PUBLICATIONS - continued

Mary Stearns Parshley

22.	Coleman, C. C., Jr., R. A. Deterling, Jr., and M. S. Parshley	Some long-term observations on aortic homografts. Surgery, 37:64-79, Jan. 1955.
23.	Parshley, M. S. and R. A. Deterling, Jr.	The effect of storage at low temperatures on growth of adult dog aorta. A. J. Anat. 97:3:359-394, Nov. 1955.
24.	Parshley, M. S.	Factors affecting the character of the outgrowth of tissue culture from the bone marrow of adult human rib. Anat. Rec. 124:429, 1956 (abstract).
25.	Parshley, M. S.	The effect of serum from patients with the nephrotic syndrome on tissue cultures of human embryonic kidney. Anat. Rec. 127:439, 1957 (abstract).
26.	Parshley, M. S.	The tissue culture of adult tissues. Chap.17 in the "Transplantation of Tissues", Vol.II, Lyndon Peer, ed., Williams and Wilkins Co., Baltimore, pp.593-633, 1959.
27.	Simms, H. S., and M. S. Parshley	The effect of proteins and amino acids on the growth of adult tissue in vitro. Chap.7 in "Protein and Amino Acid Nutrition", A. Albanese, ed., Academic Press, New York, pp.143-195, 1959.
28.	Parshley, M. S.	Isolation of a growth inhibitor from adult connective tissue. Excerpta Med., Vol.15, No.7, Sec.I, p.662, 1961 (abstract).
29.	Parshley, M. S.	Effect of growth inhibitors from adult connective tissue on growth in vitro of a series of human tumors. Excerpta Med., Vol.16, No.9, p.814, 1962.
30.	Parshley, M. S., and I. Mandl	Separation and study of a connective tissue constituent inhibitory to the growth in vitro of tumor cell strains. Proc. Am. Soc. Cancer Res., 4:1:50, 1963.
31.	Parshley, M. S.	Effect of inhibitors from adult connective tissue on growth of a series of human tumors in vitro. Cancer Res. 25:387-399, 1965

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PUBLICATIONS - continued

Mary Stearns Parshley

12. Deterling, R. A., Jr., C. C. Coleman, Jr., and Parshley, M. S. — A preliminary report on experimental studies of the frozen homologous aortic graft. N. Y. Med. 6:19-22, 1950.

13. Deterling, R. A., Jr., C. C. Coleman, Jr., and Parshley, M. S. — Experimental studies of the frozen homologous aortic graft. Surgery 29:419-440, March 1951.

14. White, J. F., and M. S. Parshley — Growth in vitro of blood vessels from the bone marrow of adult chickens. Am. J. Anat. 89:321-346, 1951.

15. Coleman, C. C., Jr., R. A. Deterling, Jr., and M. S. Parshley — Experimental studies of preserved aortic homografts. Ann. Surg. 134:868-878, 1951.

16. Hui, K.K.L., E.B.C. Keefer, R. A. Deterling, Jr., J. W. Blunt and M. S. Parshley — Early results of experimental studies of the action of high intensity electrons on aortic homografts. Surgical Forum 2:255-260, 1951. W. B. Saunders Co.

17. Pate, J. W., P. Sawyer, R. A. Deterling, Jr., J. W. Blunt and M. S. Parshley — Early results in experimental use of freeze-dried arterial grafts. Surgical Forum 3:147-152, 1952. W. B. Saunders Co., Phila.

18. Deterling, R. A., Jr., and M. S. Parshley and J. W. Blunt — A critical study of present criteria governing selection of blood vessel grafts. Surgery 33:213-232, Feb. 1953.

19. Parshley, M. S., and R. A. Deterling, Jr. — The effect of storage at low temperature on growth in vitro of adult dog aorta. Anat. Rec. 115:2:357, Feb. 1953 (abstract).

20. Parshley, M. S., R. A. Deterling, Jr., and C. C. Coleman, Jr. — Tissue culture studies of blood vessel grafts. I. The cultivation in vitro of fresh normal adult aorta (dog, cat, rabbit, goat, monkey, and human). Am. J. Anat. 93:2:221-272, Sept. 1953.

21. Parshley, M. S. — The development of tubular structures in cultures of epithelium from the cortex of adult dog kidney. Anat. Rec. 118:2:452, Feb. 1954 (abstract).

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8. cont.
ments the salts, NaSCN and $NaNO_2$, will be added directly to the culture medium or to balanced salt solution in serial dilution and allowed to remain in contact with the cells for short periods of time. Cultures of freshly explanted normal human respiratory epithelium will be exposed directly to diluted fresh tobacco smoke by the same apparatus.

The effect of these substances on the cells will be determined by the following studies.

1. Growth rate studies. Effect on rate of growth will be evaluated by dye exclusion cell counts with trypan blue, and mitotic counts.

2. Morphological Studies. Studies of differences in cell morphology and in number and character of chromosomes will be made as well as histochemical preparations to demonstrate different enzyme content. Parallel cultures on coverslips in Leighton tubes will be fixed and stained with H. and E., Giemsa, Feulgen, Methyl Green and Pyronin Y to observe effect on mitosis and nucleic acid content. Enzyme content of the cells will be observed from preparations in which the cells have been reacted for sites of alkaline phosphatases, beta-glucuronidase, succinic dehydrogenase, and leucyl beta-napthylamidase activity. For chromosome studies, cultures will be treated with colchicine to halt mitosis in the metaphase, fixed, spread, stained with acetic-orcein and observed under the oil immersion objective of the microscope and photographed.

3. Biochemical Studies. The cells and culture medium will be analyzed to evaluate the differences in the metabolic by-products of the cell lines, both treated and untreated.

a. The effect on cellular respiration and glycolysis will be observed using standard Warburg techniques. In particular glucose disappearance and lactic acid production in the used culture medium will be estimated by the methods of Trevelyan and Harrison (Biochem. J., 50:299, 1952) and Hullin and Noble (Biochem. J., 55:289, 1953).

b. The cells will be fractionated in a Spinco L2 ultracentrifuge and the mitochondrial fraction extracted and studied in the Warburg apparatus by the method of Umbreit (Manometric Techniques and Tissue Metabolism, Chap. I) and the ratios of oxygen uptake to phosphorus utilization will be estimated and compared.

c. Differences in protein patterns of the metabolic products of the cells will be established by acrylamide gel electrophoresis.

d. The enzymatic profiles of both cells and utilized culture medium will be studied with special reference to proteolytic enzyme activity using chromagenic substrates and modifications of the Bratton-Marshall method (Goldberg, Pineda, and Rutenburg, Am. J. Clin. Path., 32:571, 1959; Blackwood and Mandl, Anal. Biochem., 2: 370, 1961).

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BIOASSAY, CARCINOGENESIS and TISSUE CULTURE

NO. 630

THE COUNCIL FOR TOBACCO RESEARCH - U.S.A.

633 THIRD AVENUE
NEW YORK, N. Y. 10017

COMMITTEE:
Dr. Doosli, Chm.
Dr. Sommers
Dr. Reimann
Dr. Little

Application For Research Grant

Date: August 10, 1967

1. Name of Investigator(s): (include Title and Degrees): Mary Stearns PARSHLEY, Ph.D.
Assistant Professor of Anatomy in Obstetrics & Gynecology

2. Institution & Address: Columbia University
College of Physicians & Surgeons

630 West 168th Street
New York, N. Y. 10032

3. Short Title of Project:

EFFECT OF CONSTITUENTS OF TOBACCO SMOKE ON NORMAL AND MALIGNANT HUMAN RESPIRATORY EPITHELIUM IN VITRO.

4. Proposed Starting Date: November 1, 1967

5. Anticipated Duration of this Specific Study: Although some meaningful results should be obtained by the end of the first year, it is expected that an additional period will be required.

6. Brief Description of Objectives or Specific Aims:

There is an increasing emphasis on tobacco smoke as a contributory factor to the development of lung cancer. Tobacco products, the polycyclic aromatic hydrocarbons in particular, have been shown to induce or enhance neoplastic transformation in laboratory animals (4,9,15). On the other hand some constituents, namely the monocarboxylic acids, have been reported to have an anti-tumor effect (12). There is little precise knowledge of the qualitative and quantitative effects on normal respiratory epithelium of the nearly 300 organic and inorganic compounds reported as constituents of tobacco smoke (4,8). These include metals, hydrocarbons, alkaloids chiefly nicotine, nitrogen products, and volatile elements. Either similar factors found in polluted air or still other factors must be responsible for the occurrence of lung cancer in non-smokers, and the higher incidence of this disease among male smokers. A great deal of study has been devoted to the biological activity of tobacco tars or condensates with emphasis on the polycyclic hydrocarbons which are present only in traces (1,2,5,6,9,15). Not only has it been shown that these hydrocarbons are not specifically carcinogenic for epithelium (6,9), but the fact that fractions of smoke condensate not containing hydrocarbons also produce neoplastic changes in lung epithelium has been demonstrated (6,9). Most animal experiments deal with the carcinogenic effect on skin of smoke condensates and their fractions (4,7,8,15). Studies in which animals actually inhaled smoke gave inconsistent results (7). The skin is quite different from the mucus-coated respiratory epithelium and apparently more sensitive to the polycyclic hydrocarbons. Although nicotine content has been considered to be detrimental to the cleansing activity of the respiratory cilia (3), very little is established as to the local biological effect of nicotine (4). Little attention has been paid to the volatile substances such as carbon monoxide, hydrogen cyanide, and nitrogen oxides, present in many times higher concentration than that considered to be "safe" in industry (8,14). It is possible that neoplastic changes in normal respiratory epithelium

(cont. on p.1a)

7. Give a Brief Statement of your Working Hypothesis:

If the development of malignancy in normal human respiratory epithelium is the result of an interference with the oxygen supply and normal respiration, a simulation

(cont. on p. 1a)

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CURRICULUM VITAE

Mary Stearns Parshley
Assistant Professor of Anatomy in Obstetrics and Gynecology
College of Physicians and Surgeons, Columbia University
630 West 168th Street, New York, New York 10032

R R R

Married: Thomas Fredricson Parshley, New York City, April 15, 1938
Child: Elisabeth Stearns Parshley, born June 5, 1947

Academic Background:

Smith College, A.B. with High Honors 1933 (Zoology)
University of Pennsylvania, M.A. 1935 (Anatomy, Medical Sciences)
University of Pennsylvania, Ph.D. 1938 (Anatomy, Medical Sciences)
Travelling Fellow from Smith College at the University of Penna. 1934-1938 (Wilder, Nicolson, and Fine fellowships).
University Scholar, University of Pennsylvania, 1935-1936.
Bennett Fellow, University of Pennsylvania, 1936-1937.

Professional Experience:

1. Laboratory assistant, Willard Parker Hospital, New York City, 1933-1934.
2. Fellow in Anatomy, University of Pennsylvania, 1938-1939. Finney-Howell postdoctoral research Fellow from the Johns Hopkins University, 1938-1939.
3. Research Assistant in Pathology, Columbia University, 1940-1945. Research Associate in Pathology, Columbia University, 1945-1949.
4. Research Associate in Surgery, Columbia University, 1949-1963. Assistant Professor of Anatomy in Surgery, Columbia University, 1963-1965.
5. Lecturer in Biology, Hunter College Graduate School, 1957-1963.
6. Assistant Professor of Anatomy in Obstetrics and Gynecology, Columbia University, 1965-

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Summer:
1. Smith Scholar, Marine Biological Laboratory, Woods Hole, Mass. 1932.
2. Laboratory Assistant, St. John's Hospital, Brooklyn, New York, 1934.

World War II: Office of Scientific Research and Development, 1942-1945. (Certificate, O.S.R.D., bronze plaque, Columbia University).

Special Fields of Interest: Microscopic Anatomy and Cell Physiology. The study of living cells and tissues by the Clark-Sandison rabbit's ear chamber method, and by a variety of tissue culture techniques. Wound healing, regeneration of connective tissue, skin and blood vessels, tissue transplantation, atherosclerosis, cancer research.

Societies and Committees: Phi Beta Kappa, Sigma Xi, AAAS, Am. Assn. Anat., Physiol. Soc., Phila., Tissue Culture Assn., Am. Heart Assn., Am. Assn. Study of Arteriosclerosis, Am. Soc. Cell Biol., Am. Assn. Cancer Research. Corresponding Sec., Tissue Culture Assn., 1946-1952, Member Course Committee and Registrar Tissue Culture Assn. Summer Course, 1946-1964.

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12. Supporting Data:

A. Previous work done in this or related fields. The principal investigator has carried on extensive studies of the behavior of normal and malignant cells in rabbit's ear chambers and in tissue cultures. In collaboration with H. S. Simms several hundred biological substances and organic and inorganic chemicals were tested for their effect on growth of normal epithelium and connective tissue cells. More recently growth stimulating and growth inhibiting materials have been extracted from normal adult connective tissue and tested for effect on growth of human tumor biopsies, Rous sarcoma, and many lines of normal and malignant human and animal cells initiated in this laboratory and maintained in conrinuous cultivation. These materials were also tested against animal tumors in vivo, Sarcoma-180 in the mouse and Flexner-Jobling carcinoma in the rat and against heterologously transplanted human ovarian carcinoma in conditioned rats. The inhibitory material reduced the growth of malignant cells in tissue culture from 75-100%. Collateral studies showed that these factors inhibited the growthof animal tumors also. Recently by using different methods of fractionation we have separated materials with different growth inhibitory properties. We have obtained substances with specific inhibition for malignant fibroblasts in vitro and in vivo in one case, and materials primarily effective against malignant epithelium in another. The latter factors inhibited the same line of highly malignant ovarian carcinoma cells in tissue culture and also in animals when transplanted heterologously into conditioned weanling rats. Active specific growth stimulating and growth inhibiting materials have been separated from crude extracts by ion-exchange DEAE-cellulose chromatography and by gel filtration on Sephadex-G200 and Biogel-300. At the present time biochemical analysis is in progress to determine the exact chemical nature of these inhibitors.

B. Six most pertinent recent references. (Reprints of Cancer Res. & Nature papers included.)

Parshley, M. S. Tissue Culture of Adult Tissue. Chap. 17 in Vol. II of the "Transplantation of Tissues", ed. by L. Peer. Williams & Wilkins & Co. Baltimore 1959.

Simms, H. S., and Parshley, M. S. The effect of proteins and other substances on the growth of adult tissue in vitro. Chap. 7 in "Protein and Amino Acid Nutrition", ed. by A. Albanese. Academic Press. New York, 1959.

Parshley, M. S., and Mandl, I. Separation and study of a connective tissue constituent inhibitory to the growth in vitro of tumor cell strains. Am. Assoc. for Cancer Res. Proc., 4:1:50, 1963.

Parshley, M. S. Effect of inhibitors from adult connective tissue on growth of a series of human tumors in vitro. Cancer Research, 25:387, 1965.

Parshley, M. S., and Mandl, I. Inhibition of malignant cells in vitro by a component of normal adult connective tissue. Nature, 208:800, 1965.

Parshley, M. S., Mandl, I., and Manahan, J. Separation and in vitro study of tumor cell inhibitors. Tissue Culture Assn. Proc., San Francisco, June, 1966.

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